Alemtuzumab long-lasting immunological effects: a 48 months follow-up observation

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Objective: To perform phenotypic and functional analysis of CD4+ T cell subsets and immunologically relevant molecules mRNA serum levels after alemtuzumab treatment in relapsing remitting multiple sclerosis (RRMS) patients for a 48 months period.

Background: Alemtuzumab, a highly effective monoclonal antibody in RRMS, determines a long-standing lymphopenia, mainly of the T CD4+ cells subset.

Design and methods: We enrolled 29 alemtuzumab-treated RRMS patients from 6 European sites involved in the CARE-MS I and CARE-MS II trials in a multicenter follow-up. Patients received two course of alemtuzumab at month 0 and 12. Clinical and immunological evaluation were performed at months 0, 6, 12, 18, 24, 36 and 48. The percentages of Treg, Th1 and Th17 cells in the peripheral blood mononuclear cells (PBMC) were evaluated by FACS analysis. mRNA levels of cytokines, chemokines, chemokine receptors and transcriptional factors with pro-inflammatory (IL-1β, IL-2, IL-6, IL-12, IL-17A, IL-17F, IL-21, IL-22, IL-23, IL-26, IFN-γ, Tbet, RORC, TNF-α, CCR3, CCR4, CCR5, CCR6, CXCR3, CXCL10, CCL20, VLA4) or anti-inflammatory function (IL-10, IL-27, TGF-β and FoxP3) were quantified by TaqMan® low density array(TLDA) real-time polymerase chain reaction in whole blood. Treg suppressor activity on Myelin basic protein(MBP)-specific Th17 and Th1 cells was assessed by IL-17 and IFN-γ ELISPOT on total PBMC and PBMC depleted of CD25highT cells.

Results: In the PBMC, the percentage of CD4+ lymphocytes decreased and returned to basal levels only at month 48. Th1 and Th17 cells decreased after alemtuzumab and remained low till month 48. Treg cells percentage significantly increased at Month 24 and then slightly decreased, whereas Treg cells suppressive function significantly increased at Month 24 and persisted till month 48. No patient received further alemtuzumab courses after the first two years.

Conclusions: Alemtuzumab long-lasting therapeutic effect in RRMS involves a shift in the cytokine balance towards inhibition of inflammation and it is associated with a reconstitution of the CD4 T-cell subsets, involving the expansion of Treg cells with increased suppressive function and a reduced response against myelin antigen.

Disclosure:

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